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Substitute for Form 1449/A/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary)				Complete if Known	
				Application No.	09/641,327
				Filing Date	08/18/2000
				First Named Inventor	Agoston et al.
				Group Art Unit	1616
				Examiner Name	Qazi, Sabiha Naim
Sheet 1 of 16				Attorney Docket Number 05213-0730 (43170-21969)	

U.S. PATENT DOCUMENTS

Examiner Initials	Cite No. ¹	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number ²	Kind Code ³ (if known)			
	1	2,584,271		Huffman	02/05/1952	
	2	2,846,453		Hoehn	08/05/1958	
	3	3,410,879		Smith et al.	11/12/1968	
	4	3,470,218		Farah	09/30/1969	
	5	3,492,321		Crabbe	01/27/1970	
	6	3,496,272		Kruger (Identifier only)	02/17/1970	
	7	3,956,348		Hilscher	05/11/1976	
	8	4,172,132		Draper et al.	10/23/1979	
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	11	4,522,758		Ward et al.	06/11/1985	
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	18	5,621,124		Seilz et al.	04/15/1997	
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	20	5,661,143		D'Amato et al.	08/26/1997	
	21	5,892,069		D'Amato et al.	04/06/1999	
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	23	6,136,992		Ram et al.	10/24/2000	
	24	6,200,966	B1	Stewart	03/13/2001	

Examiner Signature	Sabiha Qazi	Date Considered	10/1/02
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				Group Art Unit	1616	
				Examiner Name	Qazi, Sabiha Naim	
Sheet	2	of	16	Attorney Docket Number		05213-0730 (43170-21969)
U.S. PATENT DOCUMENTS						
Examiner Initials	Cite No. ¹	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
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502	25	6,239,123	B1	Green et al.	05/29/2001	

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Sheet 3 of 16				Attorney Docket Number		05213-0730 (43170-219693)

FOREIGN PATENT DOCUMENTS

Examiner Initials	Cite No. ¹	Foreign Patent Document			Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶
		Office ³	Number ⁴	Kind Code ⁵ (if known)				
	26	DE	1907330		Sandoz Ltd. (Identifier only)	10/23/1969		
	27	DE	3625315		Schering A.-G (Identifier only)	01/28/1998		
SO	28	WO	90/15816	A1	The UpJohn Company	12/27/1990		
	29	WO	93/03729		Research Corporation Technologies, Inc.	03/04/1993		
	30	WO	95/04535		The Children's Medical Center Corporation	02/16/1995		
	31	WO	98/40398		Pharm-Eco Laboratories, Inc.	09/17/1998		

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Page 32 missing	32	Author: Title: Lioipristone/(1-[4-(Dimethylamino)phenyl]-17-hydroxy-17-(3-hydroxy-1-propenyl) estro-4,9-diene-3-one; AK 98734 Pub: Dict. of Drugs (1990), Dict. of Steroids (1991), Dict. of Org. Vol/Iss: Pages: 2 Date: ? Cmpds (6th Ed) (1996), Dict. of Pharm. Agents (1997)	
	33	Author: Title: (paragraphs 583-584) Pub: The Merck Index 11th Edition Vol/Iss: Pages: 88 Date: 1989	
50	34	Author: ADAMS, E.F. et al. Title: Steroidal regulation of oestradiol-17B dehydrogenase activity of the human breast cancer cell line MCF-7 Pub: Journal of Endocrinology Vol/Iss: 188 (1) Pages: 149-154 Date: 07/1988	
	35	Author: AIZU-YOKOTA et al. Title: Natural Estrogens Induce Modulation of Microtubules in Chinese Hamster V79 Cells in Culture Pub: Cancer Research Vol/Iss: 55 Pages: 1863-1868 Date: 05/01/95	
	36	Author: ATTALIA et al. Title: 2-Methoxyestradiol Arrests Cells in Mitosis without Depolarizing Tubulin Pub: Biochemical and Biophysical Research Communications Vol/Iss: 228 Pages: 467-473 Date: 1996	
	37	Author: AYALA et al. Title: The Induction of Accelerated Thymic Programmed Cell Death During Polymicrobial Sepsis: Control by Corticosteroids but not Tumor Necrosis Factor (Abstract only) Pub: Shock Vol/Iss: 3 (4) Pages: 259-267 Date: 04/1995	
	38	Author: BANIK et al. Title: Orally Active Long-Acting Estrogen (3-(2-propynyloxy)-estra-1,3,5,(10)-triene-17. beta.-ol trimethylacetate) (Identifier only) Pub: Steroids Vol/Iss: 16 (3) Pages: 289-296 Date: 1970	

Examiner Signature	SABIHA QAZI	Date Considered	10/1/02
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OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS					
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	39	Author: BARDON et al. Title: Steroid Receptor-Mediated Cytotoxicity of an Antiestrogen and an Antiprogesterin in Breast Cancer Cells (Abstract only) Publ: Cancer Research Vol/Iss: 47 (5) Pages: 1441-1448 Date: 03/01/87			
	40	Author: BHAT et al. Title: Estradiol-induced Mitotic Inhibition in the Bursa of Fabricius of Male Domestic Duckling Publ: Mikroskopie Vol/Iss: 39 Pages: 113-117 Date: 05/1982			
SR	41	Author: BLAGOSKLONNY et al. Title: Raf-1/bcl-2 Phosphorylation: A Step from Microtubule Damage to Cell Death Publ: Cancer Research Vol/Iss: 57 Pages: 130-135 Date: 01/01/97			
	42	Author: BLICKENSTAFF et al. Title: Estrogen-Catharanthus (Vinca) Alkaloid Conjugates Publ: Cytotoxic Estrogens in Hormone Receptive Tumors Vol/Iss: Pages: 89-105 Date: 1980			
	43	Author: BOYE et al. Title: 185. Deaminocolchiciny Methyl Ether: Synthesis from 2,3,4,4'-Tetramethoxybiphenyl Publ: Helvetica Chimica Acta Vol/Iss: 72 Pages: 1690-1696 Date: 1989			
	44	Author: BRODIE, A.M. Title: Aromatase Inhibitors in the Treatment of Breast Cancer (Abstract only) Publ: Journal of Steroid Biochemistry and Molecular Biology Vol/Iss: 49 (4-6) Pages: 281-287 Date: 06/1994			
	45	Author: BROSENS et al. Title: Comparative Study of the Estrogenic Effect of Ethinylestradiol and Mestranol on the Endometrium Publ: Laboratory for Gynecological Physiopathology Vol/Iss: 14 (6) Pages: 679-685 Date: 12/01/76			

Examiner Signature	Sabiha Qazi	Date Considered	10/1/02
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				Group Art Unit	1616
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Sheet	6	of	16	Attorney Docket Number	05213-0730 (43170-219693)

OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS

Examiner Initials	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T ²
	46	Author: CASTAGNETTA, L. et al. Title: Simple Approach to Measure Metabolic Pathways of Steroids in Living Cells Publ: <u>Journal of Chromatography</u> Vol/Iss: 572 Pages: 25-39 Date: 12/06/91	
SD	47	Author: CHASSEROT-GOLAZ et al. Title: Biotransformation of 17.beta.-hydroxy-11.beta.-(4-dimethylaminophenyl) 17.alpha.1-propynyl-estra-4,9-diene-3-one (RU486) in Rat Hepatoma Variants (Identifier only) Publ: <u>Biochemical Pharmacology</u> Vol/Iss: 46 (11) Pages: 2100-2103 Date: 01/01/93	
	48	Author: CHEN et al. Title: A New Synthetic Route to 2- and 4-Methoxyestradiols by Nucleophilic Substitution Publ: <u>Steroids</u> Vol/Iss: 47 (1) Pages: 63-66 Date: 01/1986	
	49	Author: CHEN et al. Title: Synthesis of 11.beta.-(4-dimethylaminophenyl)-17.beta.-hydroxy-17.alpha.-(1-propyl) estro-4, 9-dien-3-one (RU486) (Identifier only) Publ: <u>Nanjing Yaoxueyuan Xuebao</u> Vol/Iss: 17 (4) Pages: 282-285 Date: 1986	
	50	Author: COHEN et al. Title: Novel Total Synthesis of (+)-Estrone 3-Methyl Ether, (+)-13B-Ethyl-3-methoxygona-1,3,5(10-triene-17-one, and (+)-Equilenin 3-Methyl Ether Publ: <u>The Journal of Organic Chemistry</u> Vol/Iss: 6 Pages: 681-685 Date: 03/21/75	
	51	Author: COLLINS et al. Title: The Structure and Function of Estrogens. XI* Synthesis of (+/-)-7(8-11 α) abeo-Estradiol and its 9,11-Didehydro Derivative Publ: <u>Aust. Journal of Chemistry</u> Vol/Iss: 45 Pages: 71-97 Date: 1992	
	52	Author: CRUM, R. et al. Title: A New Class of Steroids Inhibits Angiogenesis in the Presence of Heparin or a Heparin Fragment Publ: <u>SCIENCE</u> Vol/Iss: 230 Pages: 1375-1378 Date: 12/20/85	

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Sheet 7 of 16	Attorney Docket Number		05213-0730 (43170-219658)		

OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS

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	53	Author: CUMMINGS et al. Title: Apoptosis Publ: The American Journal of Surgical Pathology Vol/Iss: 21 (1) Pages: 88-101 Date: 1997	
	54	Author: CUSHMAN et al. Title: Synthesis, Antitubulin and Antimitotic Activity, and Cytotoxicity of Analogs of 2-Methoxyestradiol, an Endogenous Mammalian Metabolite of Estradiol that Publ: Journal of Medical Chemistry Vol/Iss: 38 (12) Pages: 2041-2049 Date: 1995	
SQ	55	Author: CUSHMAN et al. Title: Synthesis of Analogs of 2-Methoxyestradiol with Enhanced Inhibitory Effects of Tubulin Polymerization and Cancer Cell Growth Publ: Journal of Medical Chemistry Vol/Iss: 40 (15) Pages: 2323-2334 Date: 1997	
	56	Author: D'AMATO et al. Title: 2-Methoxyestradiol, an Endogenous Mammalian Metabolite, Inhibits Tubulin Polymerization by Interacting at the Colchicine Site Publ: Proceedings of the National Academy of Science USA Vol/Iss: 91 Pages: 3964-3968 Date: 04/1994	
	57	Author: DVIR et al. Title: Thin-layer Chromatography of DANSYL-oestrogens Publ: Journal of Chromatography Vol/Iss: 52 Pages: 505-506 Date: 11/04/70	
	58	Author: EPE et al. Title: Microtubular Proteins as Cellular Targets for Carcinogenic Estrogens and Other Carcinogens Publ: Mechanisms of Chromosome Distribution and Aneuploidy Vol/Iss: Pages: 345-351 Date: 1989	
	59	Author: EVANS et al. Title: A Convergent Total Synthesis of (+)- Colchicine and (+)-Desacetamidoisocolchicine Publ: Journal of the American Chemical Society Vol/Iss: 103 Pages: 5813-5821 Date: 09/23/81	

Examiner Signature	Sabiha Qazi	Date Considered	10/1/02
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	60	Author: FISHMAN, J. Title: Synthesis of 2-Methoxyestrogens Publ: <u>Journal of the American Chemical Society</u> Vol/Iss: 80 Pages: 1213-1216 Date: 03/05/98			
	61	Author: FITZGERALD Title: Molecular Features of Colchicine Associated with Antimitotic Activity and Inhibition of Tubulin Polymerization Publ: <u>Biochemical Pharmacology</u> Vol/Iss: 25 Pages: 1383-1387 Date: 06/15/76			
50	62	Author: FOTSIS et al. Title: The Endogenous Oestrogen Metabolite 2-Methoxyoestradiol Inhibits Angiogenesis and Suppresses Tumour Growth Publ: <u>Nature</u> Vol/Iss: 368 Pages: 237-239 Date: 03/17/94			
	63	Author: GETAHUN et al. Title: Synthesis of Alkoxy-Substituted Diaryl Compounds and Correlation of Ring Separation with Inhibition of Tubulin Polymerization: Differential Enhancement of Inhibitory Effects Under Suboptimal Polymerization Publ: <u>Journal of Medical Chemistry</u> Vol/Iss: 35 (6) Pages: 1058-1067 Date: 03/20/92			
	64	Author: GROSS et al. Title: Inhibition of Tumor Growth, Vascularization, and Collagenolysis in the Rabbit Cornea by Medroxyprogesterone Publ: <u>Proceedings of the National Academy of Science USA</u> Vol/Iss: 78 (2) Pages: 1176-1180 Date: 02/1981			
	65	Author: GUANGRONG et al. Title: Effect of Components of Crowth Ether Copper(I)Iodide Mixed Catalyst on Nucleophilic Substitution of Bromoestrogen (Abstract No. 195225) Publ: <u>Chemical Abstracts</u> Vol/Iss: 111 (21) Pages: 818, Column 1 Date: 11/20/89			
	66	Author: HALDAR et al. Title: Bc12 is the Guardian of Microtubule Integrity Publ: <u>Cancer Research</u> Vol/Iss: 57 Pages: 229-233 Date: 01/15/97			

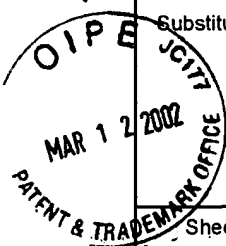
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Agoston et al.

Group Art Unit

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	67	Author: HAMEL et al. Title: Interactions of 2-Methoxyestradiol, an Endogenous Mammalian Metabolite, with Unpolymerized Tubulin and with Tubulin Polymers Publ: <u>Biochemistry</u> Vol/Iss: 35 (4) Pages: 1304-1310 Date: 1996	
	68	Author: HARTLEY-ASP et al. Title: Diethylstilbestrol Induces Metaphase Arrest and Inhibits Microtubule Assembly Publ: <u>Mutation Research</u> Vol/Iss: 143 (4) Pages: 231-235 Date: 08/1985	
SLQ	69	Author: HE et al. Title: A Versatile Synthesis of 2-Methoxyestradiol, an Endogenous Metabolite of Estradiol which Inhibits Tubulin Polymerization by Binding to the Colchicine Binding Site Publ: <u>Bioorganic & Medicinal Chemistry Letters</u> Vol/Iss: 4 (14) Pages: 1724-1728 Date: 1994	
	70	Author: HUBER et al. Title: Tubulin Binding of Conformationally Restricted Bis-Aryl Compounds Publ: <u>Bioorganic & Medicinal Chemistry Letters</u> Vol/Iss: 1 (5) Pages: 243-246 Date: 1991	
	71	Author: JOSEFSSON et al. Title: Suppression of Type II Collagen-Induced Arthritis by the Endogenous Estrogen Metabolite 2-Methoxyestradiol Publ: <u>Arthritis & Rheumatism</u> Vol/Iss: 40 (1) Pages: 154-163 Date: 01/1997	
	72	Author: KABARITY et al. Title: Further Investigations on the cytological effects of some contraceptives Publ: <u>Mutation Research</u> Vol/Iss: 135 Pages: 181-188 Date: 1984	
	73	Author: KELLY et al. Title: The Stimulation of Prostaglandin Production by Two Antiprogestosterone Steroids in Human Endometrial Cells (Abstract only) Publ: <u>Journal of Clinical Endocrinology Metabolism</u> Vol/Iss: 62 (6) Pages: 1116-1123 Date: 06/1986	

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Sabiha Qazi

Date
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	74	Author: KLAUBER et al. Title: Inhibition of Angiogenesis and Breast Cancer in Mice by the Microtubule Inhibitors 2-Methoxyestradiol and Taxol Publ: Cancer Research Vol/Iss: 57 Pages: 81-86 Date: 01/01/97	
	75	Author: LEBRAS, J. et al. Title: Activation and Regioselective Ortho-Functionalization of the A-Ring of B-Estradiol Promoted by "Cp*Ir": An Efficient Organometallic Procedure for the Synthesis of 2-Methoxyestradiol Publ: Organometallics Vol/Iss: 16 Pages: 1765-1771 Date: 1997	
SC	76	Author: LIN et al. Title: Interactions of Tubulin with Potent Natural and Synthetic Analogs of the Antimitotic Agent Combretastatin: A Structure-Activity Study Publ: Molecular Pharmacology Vol/Iss: 34 (2) Pages: 200-208 Date: 08/1988	
	77	Author: LINCOLN et al. Title: Conformation of Thiocolchicine and Two B-Ring-Modified Analogues Bound to Tubulin Studied with Optical Spectroscopy Publ: Biochemistry Vol/Iss: 30 (5) Pages: 1179-1187 Date: 02/05/91	
	78	Author: LOTTERING et al. Title: Effects of the 17 β -Estradiol Metabolites on Cell Cycle Events in MCF-7 Cells Publ: Cancer Research Vol/Iss: 52 Pages: 5926-5932 Date: 11/01/92	
	79	Author: LOTTERING et al. Title: 17 β -Estradiol Metabolites Affect Some Regulators of the MCF-7 Cell Cycle Publ: Cancer Letters Vol/Iss: 110 Pages: 181-186 Date: 1996	
	80	Author: MAYOL et al. Title: Ethynylestradiol-Induced Cell Proliferation in Rat Liver Involvement of Specific Populations of Hepatocytes (Abstract only) Publ: Carcinogenesis Vol/Iss: 12 (12) Pages: 2381-2388 Date: 1992	

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Sabiha Qazi

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¹Unique citation designation number. ²See attached Kinds of U.S. Patent Documents. ³Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴For Japanese patent document, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶Applicant is to place a check mark here if English language translation is attached.

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary)				Application No.	09/641,327
				Filing Date	08/18/2000
				First Named Inventor	Agoston et al.
				Group Art Unit	1616
				Examiner Name	Qazi, Sabiha Naim
Sheet	11	of	16	Attorney Docket Number	05213-0730 (43170-21969)

OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS

Examiner Initials	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	L ²
	81	Author: MEIKRANTZ et al. Title: Apoptosis and the Cell Cycle Publ: <u>Journal of Cellular Biochemistry</u> Vol/Iss: 58 Pages: 160-174 Date: 06/1995	
SB	82	Author: MILLER et al. Title: Synthesis and Structure-Activity Profiles of A-Homoestrans, the Estratropenes Publ: <u>Journal of Medicinal Chemistry</u> Vol/Iss: 40 Pages: 3836-3841 Date: 1997	
	83	Author: MORGAN et al. Title: Calcium and Oestrogen Interactions upon the Rat Thymic Lymphocyte Plasma Membrane Publ: <u>Biochemical and Biophysical Research Communications</u> Vol/Iss: 72 (2) Pages: 663-672 Date: 09/20/76	
	84	Author: MUKHOPADHYAY et al. Title: Induction of Apoptosis in Human Lung Cancer Cells after Wild-Type p53 Activation by Methoxyestradiol Publ: <u>Oncogene</u> Vol/Iss: 14 Pages: 379-384 Date: 1997	
	85	Author: MUKUNDAN et al. Title: Liver Regeneration in Oral Contraceptive Treated Female Rats - Effects of Moderate Malnutrition Publ: <u>Hormone and Metabolic Research</u> Vol/Iss: 16 Pages: 641-645 Date: 12/1984	
	86	Author: NAKAGAWA-YAGI et al. Title: The Endogenous Estrogen Metabolite 2-Methoxyestradiol Induces Apoptotic Neuronal Cell Death <i>In Vitro</i> Publ: <u>Life Sciences</u> Vol/Iss: 58 (17) Pages: 1461-1467 Date: 1996	
	87	Author: NAKAMURA et al. Title: Studies on the Total Synthesis of <i>dl</i> -Colchicine. I. Synthesis of 3-Hydroxy-9, 10, 11-trimethoxy-1,2,3,4,6,7-hexahydro-5H-dibenso[a,c] cycloheptatrien-5-one Publ: <u>Chemical and Pharmaceutical Bulletin</u> Vol/Iss: 10 Pages: 281-290 Date: 1962	

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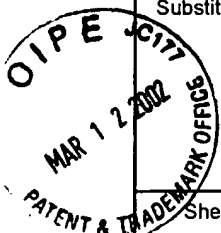
Substitute for Form 1449/A/PTO				Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary)				Application No.	09/641,327
				Filing Date	08/18/2000
				First Named Inventor	Agoston et al.
				Group Art Unit	1616 <i>#3</i>
				Examiner Name	Qazi, Sabiha Naim
Sheet	12	of	16	Attorney Docket Number	05213-0730 (43170-219693)

OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS

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<i>SA</i>	88	Author: NAMBARA et al. Title: Studies on Steroid Conjugates. III. New Synthesis of 2-Methoxyestrogens Publ: Chem. Pharm. Bulletin Vol/Iss: 18 (3) Pages: 474-480 Date: 03/1970	
	89	Author: NAPOLITANO et al. Title: 11 Beta-Substituted Estradiol Derivatives. 2. Potential Carbon-11 and Iodine-Labeled Probes for the Estrogen Receptor (Abstract only) Publ: Journal of Medical Chemistry Vol/Iss: 38 (14) Pages: 2774-2779 Date: 07/07/95	
	90	Author: NISHIGAKI et al. Title: Anti-Proliferative Effect of 2-Methoxyestradiol on Cultured Smooth Muscle Cells from Rabbit Aorta Publ: Atherosclerosis Vol/Iss: 113 Pages: 167-170 Date: 1995	
	91	Author: OCHS et al. Title: Effect of Tumor Promoting Contraceptive Steroids on Growth and Drug Metabolizing Enzymes in Rat Liver (Abstract only) Publ: Cancer Research Vol/Iss: 46 (3) Pages: 1224-1232 Date: 1986	
	92	Author: OPPOLZER et al. Title: 177. The Enantioselective Synthesis of (+)-Estradiol from 1,3-Dihydrobenzo[c] thiophene-2,2-dioxide by Successive Thermal SO ₂ -Extrusion and Cycloaddition Reactions Publ: Helvetica Chimica Acta Vol/Iss: 63 Pages: 1703-1707 Date: 1980	
	93	Author: PARTHASARATHY et al. Title: Antioxidant: A New Role for RU-486 and Related Compounds (Abstract only) Publ: Journal of Clinical Investigation Vol/Iss: 94 (5) Pages: 1990-1995 Date: 11/1994	
	94	Author: PAULL et al. Title: Identification of Novel Antimitotic Agents Acting at the Tubulin Level by Computer-assisted Evaluation of Differential Cytotoxicity Data Publ: Cancer Research Vol/Iss: 52 Pages: 3892-3900 Date: 07/15/92	

Examiner Signature	<i>Sabiha Qazi</i>	Date Considered	<i>10/2/02</i>
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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary)				Application No.	09/641,327
				Filing Date	08/18/2000
				First Named Inventor	Agoston et al.
				Group Art Unit	1616
				Examiner Name	Qazi, Sabiha Naim
Sheet	13	of	16	Attorney Docket Number	05213-0730 (43170-219693)

OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS

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	95	Author: POLI et al. Title: Tumor Necrosis Factor α Functions in an Autocrine Manner in the Induction of Human Immunodeficiency Virus Expression Publ: Proceedings of the National Academy of Science USA Vol/Iss: 87 Pages: 782-785 Date: 01/1990	
	96	Author: RAVINDRA, R. Title: Effect of Estradiol on the <i>in vitro</i> Assembly of Rat Brain Tubulin Publ: Journal of Indian Institute of Science Vol/Iss: 64 (3) Pages: 27-35 Date: 03/1983	
56	97	Author: SAKAKIBARA et al. Title: Effects of Diethylstilbestrol and its Methyl Ethers on Aneuploidy Induction and Microtubule Distribution in Chinese Hamster V79 cells Publ: Mutation Research Vol/Iss: 263 Pages: 269-276 Date: 08/1991	
	98	Author: SATO et al. Title: Effect of Estradiol and Ethynylestradiol on Microtubule Distribution in Chinese Hamster V79 Cells Publ: Chemical and Pharmaceutical Bulletin Vol/Iss: 40 (1) Pages: 182-184 Date: 01/1992	
	99	Author: SATO et al. Title: Disruptive Effect of Diethylstilbestrol on Microtubules Publ: Gann Vol/Iss: 75 Pages: 1046-1048 Date: 12/1984	
	100	Author: SAWADA et al. Title: Colchicine-Like Effect of Diethylstilbestrol (DES) on Mammalian Cells in Vitro Publ: Mutation Research Vol/Iss: 57 Pages: 175-182 Date: 05/1978	
	101	Author: SEEGERs et al. Title: Cyclic-AMP and Cyclic-GMP Production in MCF-7 Cells Exposed to Estradiol-17 Beta, Catecholestrogens and Methoxy-Estrogens in MCF-7 Cells (Meeting Abstract only) Publ: Joint MCI-1st Symposium. Third 1st International Symposium. Biology and Therapy of Breast Cancer Vol/Iss: Pages: Date: 09/25/89	

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary)				Application No.	09/641,327
				Filing Date	08/18/2000
				First Named Inventor	Agoston et al. #8
				Group Art Unit	1616
				Examiner Name	Qazi, Sabiha Naim
Sheet	14	of	16	Attorney Docket Number	05213-0730 (43170-219693)
OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS					
Examiner Initials	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published			T ²
	102	Author: SEEGERS, J.C. et al. Title: The Cytotoxic Effects of Estradiol-17B, Catecholestradiols and Methoxyestradiols on Dividing MCF-7 and HeLa Cells Publ: Journal of Steroid Biochemistry Vol/Iss: 32 (6) Pages: 797-809 Date: 1989			
	103	Author: SHARP et al. Title: Diethylstilbestrol: the Binding and Effects of Diethylstilboestrol upon the Polymerisation and Depolymerisation of Purified Microtubule Protein in vitro Publ: Carcinogens Vol/Iss: 6 (6) Pages: 865-871 Date: 06/1985			
40	104	Author: SPICER et al. Title: Catecholestrogens Inhibit Proliferation and DNA Synthesis of Porcine Granulosa Cells in Vitro: Comparison with Estradiol, 5 α -dihydrotestosterone, Gonadotropins and Catecholamines Publ: Molecular and Cellular Endocrinology Vol/Iss: 64 Pages: 119-126 Date: 1989			
	105	Author: STERNLICHT et al. Title: Colchicine Inhibition of Microtubule Assembly via Copolymer Formation Publ: The Journal of Biological Chemistry Vol/Iss: 254 (20) Pages: 10540-10550 Date: 10/25/79			
	106	Author: SUN et al. Title: Antitumor Agents. 139. Synthesis and Biological Evaluation of Thiocolchicine Analogs 5,6-Dihydro-6(S)-(acyloxy)-and 5,6-Dihydro-6(S)-[(acyloxy)methyl]-1,2,3- Publ: Journal of Medicinal Chemistry Vol/Iss: 36 Pages: 544-551 Date: 03/05/93			
	107	Author: SUNAGAWA et al. Title: Synthesis of Colchicine; Synthesis of d,l'-Demethoxydeoxy-hexahydrocolchicine Publ: Chem. Pharm. Bulletin Vol/Iss: 9 Pages: 81-83 Date: 1961			
	108	Author: TERANISHI, M. et al. Title: Methylation of Catechol Estrogen with Diazomethane Publ: Chemical and Pharmaceutical Bulletin Vol/Iss: 31 (9) Pages: 3309-3314 Date: 09/1983			

Examiner Signature	Sabiha Qazi	Date Considered	10/2/02
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¹Unique citation designation number. ²See attached Kinds of U.S. Patent Documents. ³Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴For Japanese patent document, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶Applicant is to place a check mark here if English language translation is attached.

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary)				Application No.	09/641,327
				Filing Date	08/18/2000
				First Named Inventor	Agoston et al.
				Group Art Unit	1616
				Examiner Name	Qazi, Sabiha Naim
Sheet 15 of 16	Attorney Docket Number		05213-0730 (43170-21988)		
OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS					
Examiner Initials	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published			P ²
	109	Author: TISHLER et al. Title: Microtubule-Active Drugs Taxol, Vinblastine, and Nocodazole Increase the Levels of Transcriptionally Active p53 Publ: Cancer Research Vol/Iss: 55 Pages: 6021-6025 Date: 12/15/95			
	110	Author: TSUTSUI et al. Title: Comparison of Human Versus Syrian Hamster Cells in Culture for Induction of Mitotic Inhibition, Binucleation and Multinucleation, Following Treatment with Four Aneuploidogens Publ: Toxicology in Vitro Vol/Iss: 4 (1) Pages: 75-84 Date: 1990			
gbi	111	Author: UTNE et al. Title: The Synthesis of 2- and 4-Fluoroestradiol Publ: Journal of Organic Chemistry Vol/Iss: 33 (6) Pages: 2469-2473 Date: 06/1968			
	112	Author: VAN GEERESTEIN et al. Title: Structure of 11.β.-[4-(dimethylamino)phenyl]-17.β.-hydroxy-17.α.-[2- propenyl] estro-4,9-dien-3-one (Identifier only) Publ: Acta Crystall Ogr., Sect. C: Cryst. Struct. Commun. Vol/Iss: C43 (2) Pages: 319-322 Date: 1987			
	113	Author: VAN TAMELEN et al. Title: The Synthesis of Colchicine Publ: Tetrahedron Vol/Iss: 14 Pages: 8-34 Date: 09/1961			
	114	Author: WANG, Z. et al. Title: An Optimized Synthesis of 2-Methoxyestradiol, a Naturally Occurring Human Metabolite with Anticancer Activity Publ: Synth. Commun. Vol/Iss: 28 (23) Pages: 4431-4437 Date: 1998			
	115	Author: WHEELER et al. Title: Mitotic Inhibition and Aneuploidy Induction by Naturally Occurring and Synthetic Estrogens in Chinese Hamster Cells in Vitro Publ: Mutation Research Vol/Iss: 171 Pages: 31-41 Date: 1986			

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary)				Application No.	09/641,327
				Filing Date	08/18/2000
				First Named Inventor	Agoston et al.
				Group Art Unit	1616
				Examiner Name	Qazi, Sabiha Naim
Sheet	16	of	16	Attorney Docket Number	05213-0730 (43170-21968)
OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS					
Examiner Initials	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published			T ²
SB	116	Author: WHEELER et al. Title: Mitotic Inhibition and Chromosome Displacement Induced by Estradiol in Chinese Hamsters Cells Publ: <u>Cell Motility and the Cytoskeleton</u> Vol/Iss: 7 (3) Pages: 235-247 Date: 1987			
	117	Author: YUE et al. Title: 2-Methoxyestradiol, an Endogenous Estrogen Metabolite, Induces Apoptosis in Endothelial Cells and Inhibits Angiogenesis: Possible Role for Stress-Activated Protein Kinase Signaling Pathway and Fas Expression Publ: <u>Molecular Pharmacology</u> Vol/Iss: 51 Pages: 951-952 Date: 1997			

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¹Unique citation designation number. ²See attached Kinds of U.S. Patent Documents. ³Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴For Japanese patent document, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶Applicant is to place a check mark here if English language translation is attached.

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				Application No.	09/641,327			
				Filing Date	08/18/2000 #9			
				First Named Inventor	Agoston			
				Group Art Unit	1616			
				Examiner Name	Sabiha Naim Qazi			
Sheet	1	of	3	Attorney Docket Number	05213-0730 (43170-219693)			
FOREIGN PATENT DOCUMENTS								
Examiner Initials	Cite No. ¹	Foreign Patent Document			Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	L
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SO	1	JP	63090763	A	Research Development Corp. of Japan (Abstract only)	04/21/1988		

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				Application No.	09/641,327
				Filing Date	08/18/2000
				First Named Inventor	Agoston <i>29</i>
				Group Art Unit	1616
Examiner Name	Sabiha Naim Qazi				
Attorney Docket Number	05213-0730 (43170-219693)				
Sheet	2	of	3		
OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS					
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COPY OF PAPERS ORIGINALLY FILED	2	Author: ARNOLDI et al. Title: Sweet Isovanillyl Derivatives: Synthesis and Structure-Taste Relationships of Conformationally Restricted Analogs (abstract only) Publ: Journal of Agric. Food Chem. Vol/Iss: 46(10) Pages: 4002-4010 Date: 1998			
	3	Author: AUDIER et al. Title: Orientation de la fragmentation en spectrometrie de masse par introduction de groupements fonctionnels. VII. - Etheylenecetals de ceto-2 steroides Publ: Bulletin De La Societe Chimique De France Vol/Iss: 10 Pages: 3088-3090 Date: 1965			
	4	Author: CAMBIE et al. Title: Aromatic Steroids. Part II. Chromium Trioxide Oxidation of Some Oestra-1,3-5(10)-trienes Publ: Journal of the Chemical Society Vol/Iss: 9 Pages: 1234-1240 Date: 1969			
	5	Author: FETIZON et al. Title: Synthesis of 2-keto steroids (abstract only) Publ: Bull. Soc. Chim. FR. Vol/Iss: 8 Pages: 3301-3306 Date: 1968			
	6	Author: LICHTENAUER et al. Title: Zur Behandlung des Prostata-Karzinoms Publ: Deutsches medizinisches Journal Vol/Iss: 23 Pages: 248-249 Date: 01/1972			
	7	Author: LIMANTSEV et al. Title: Effect of some estrogen structural analogs on the development of the mouse embryo (abstract only) Publ: Akush Jinekoi. Vol/Iss: 6 Pages: 55-56 Date: 1982			
	8	Author: MILLER, Thomas Title: Tubulin as a Therapeutic Target (Abstract only) Publ: Dissertations Abstracts International Vol/Iss: 5907B Pages: 3454 Date: 1998			

Examiner Signature	<i>Sabiha Qazi</i>	Date Considered	<i>10/3/02</i>
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				Filing Date	08/18/2000	
				First Named Inventor	Agoston #9	
				Group Art Unit	1616	
				Examiner Name	Sabiha Naim Qazi	
Sheet	3	of	3	Attorney Docket Number		05213-0730 (43170-219693)
OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS						
Examiner Initials	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published				
	9	Author: NUMAZAWA et al. Title: Efficient Synthesis of 2-Methoxy- and 4-Methoxy-Estrogens Publ: Journal of the Chemical Society Vol/Iss: Pages: 533-534 Date: 01/01/83				
GB	10	Author: RAO et al. Title: Structural Specificity of Estrogens in the Induction of Mitotic Chromatid Non-Disjunction in Hela Cells Publ: Experimental Cell Research Vol/Iss: 48 Pages: 71-81 Date: 1967				
	11	Author: RAO et al. Title: A Novel, Two-Step Synthesis of 2-Methoxyestradiol Publ: Synthesis Vol/Iss: Pages: 168-169 Date: 03/01/77				
	12	Author: SAKAKIBARA, KYOICHI Title: 2-Hydroxy-1,3,5(10)-estratriene derivatives (abstract only) (Identifier: XP-002186126) Publ: Chemical Abstracts Vol/Iss: 60(1) Pages: Date: 01/06/64				

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				Filing Date	08/18/2000
				First Named Inventor	Agoston et al.
				Group Art Unit	1616
				Examiner Name	S. N. Qazi, Ph.D.
Sheet	1	of	10	Attorney Docket Number	05213-0730 (43170-219693)

U.S. PATENT DOCUMENTS

Examiner Initials	Cite No. ¹	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number ⁴	Kind Code ² (if known)			
SO	1	3,166,577		Ringold et al.	01/19/1965	
1	2	3,562,260		De Ruggieri et al.	02/09/1971	

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Substitute for Form 1449/A/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary)				Complete if Known	
				Application No.	09/641,327
				Filing Date	08/18/2000
				First Named Inventor	Agoston et al. #17
				Group Art Unit	1616
Examiner Name	S. N. Qazi, Ph.D.				
Attorney Docket Number	05213-0730 (43170-219693)				
Sheet	2	of	10		

FOREIGN PATENT DOCUMENTS

Examiner Initials	Cite No. ¹	Foreign Patent Document			Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ²
		Office ³	Number ⁴	Kind Code ⁵ (if known)				
	3	WO	00/07576	A2	ENDORECHERCHE, INC	02/17/2000		
	4	WO	00/10552	A2	Global Vascular Concepts, Inc.	03/02/2000		
	5	WO	00/66095	A2	Sterix Limited	11/09/2000		
	6	WO	00/68246	A1	Research Institute for Medicine and Chemistry Inc.	11/16/2000		
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SC	8	WO	01/85755	A1	Research Institute for Medicine and Chemistry Inc. and Marsden, John	11/15/2001		
	9	JP	39-5480	B	Teikoku Hormone Mfg. Co.			No
	10	GB	857,080		Syntex S.A.	12/29/1960		
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	13	DE	2 004 516		VEB Jenapharm	09/10/1970		No
	14	WO	87/02367	A3	The Upjohn Company	04/23/1987		RECEIVED
	15	WO	88/08002	A1	The Upjohn Company	10/20/1988		OCT 15 2002

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	16	WO	98/32763	A1	SRI International	07/30/1998		
	17	WO	99/01142	A1	Hyal Pharmaceutical Corporation	01/14/1999		
SA	18	WO	99/33858	A3	SRI International	07/08/1999		
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	20	JP	41 000100 (XP-002200990)	A	Dainippon Pharmaceutical Co., Ltd. (abstract only)	01/07/1966		
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	22	Author: ABOULWafa et al. Title: Synthesis and evaluation for uterotrophic and antiimplantation activities of 2-substituted estradiol derivatives Publ: Steroids Vol/Iss: 57 Pages: 199-204 Date: 04/1992				
	23	Author: BLICKENSTAFF et al. Title: SYNTHESIS OF SOME ANALOGS OF ESTRADIOL Publ: Steroids Vol/Iss: 46 (4,5) Pages: 889-902 Date: 10/1985				
	24	Author: BRANDI et al. Title: Bone endothelial cells as estrogen targets (Abstract only) Publ: Calcif. Tissue Int. Vol/Iss: 53 (5) Pages: 312-317 Date: 1993				
	25	Author: BRUEGGEMEIER et al. Title: 2-Methoxymethylestradiol: a new 2-methoxy estrogen analog that exhibits antiproliferative activity and alters tubulin dynamics Publ: Journal of Steroid Biochemistry & Molecular Biology Vol/Iss: 78 Pages: 145-156 Date: 2001				
	26	Author: CRABBE, P. Title: Cotton effect of the styrene chromophore (Abstract only) Publ: Chem. Ind. Vol/Iss: 27 Pages: 917-918 Date: 1969				
	27	Author: DUBEY et al. Title: Methoxyestradiols Mediate the Antimitogenic Effects of Estradiol on Vascular Smooth Muscle Cells via Estrogen Receptor-Independent Mechanisms Publ: Biochemical and Biophysical Research Communications Vol/Iss: 278 Pages: 27-33 Date: 2000				
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	29	Author: EMONS et al. Title: Modulation der hypophysaren Sekretion von Luteinisierendem Hormon (LH) durch Ostrogene Publ: FOCUS MHL Vol/Iss: 3 Pages: 221-228 Date: 1986			
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SD	31	Author: FRASER et al. Title: Angiogenesis and its control in the female reproductive system (Abstract only) Publ: British Medical Bulletin Vol/Iss: 56 (3) Pages: 787-797 Date: 2000			
	32	Author: GANDHI et al. Title: Mannich reaction of estrone Publ: Journal of Indian Chem. Soc. Vol/Iss: 39 Pages: 306-308 Date: 1962			
	33	Author: HAHNEL et al. Title: THE SPECIFICITY OF THE ESTROGEN RECEPTOR OF HUMAN UTERUS Publ: Journal of Steroid Biochemistry Vol/Iss: 4 Pages: 21-31 Date: 1973			
	34	Author: HE et al. Title: NOVEL CYTOKINE RELEASE INHIBITORS. PART II: STEROIDS Publ: Bioorganic & Medicinal Chemistry Letters Vol/Iss: 8 Pages: 2825-2828 Date: 1998			
	35	Author: HEJAZ et al. Title: Synthesis and Biological Activity of the Superestrogen (E)-17-Oximino-3-O-sulfamoyl-1,3,5(10)-estratriene: X-ray Crystal Structure of (E)-17-Oximino-3-hydroxy-1,3,5(10)-estratriene Publ: Journal of Medicinal Chemistry Vol/Iss: 42 (16) Pages: 3188-3192 Date: 1999			

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	36	Author: HOLKER et al. Title: The Reactions of Estrogens with Benzeneseleninic Anhydride and Hexamethyldisilazane Publ: J. Chem. Soc. Perkin Trans. Vol/Iss: 1 Pages: 1915-1918 Date: 1982			
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	39	Author: IRIARTE et al. Title: Steroids (XCIV). Synthesis of 2-methyl and 1,2-dimethyl estrogens (Abstract only) Publ: Tetrahedron Vol/Iss: 3 Pages: 28-36 Date: 1958			
	40	Author: JAGGERS et al. Title: Potent Inhibitory effects of steroids in an in vitro model of angiogenesis (Abstract only) Publ: Journal of Endocrinology Vol/Iss: 150 (3) Pages: 457-464 Date: 1996			
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	47	Author: MICHEL et al. Title: Inhibition of synaptosomal high-affinity uptake of dopamine and serotonin by estrogen agonists and antagonists (Abstract only) Publ: Biochem. Pharmacol. Vol/Iss: 36 (19) Pages: 3175-3180 Date: 1987			
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	49	Author: MUECK et al. Title: Angiogenetic and anti-angiogenetic effects of estradiol and its metabolites (Abstract only) Publ: Journal of Clinical and Basic Cardiology Vol/Iss: 4 (2) Pages: 153-155 Date: 2001			

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	60	Author: SPYRIOUNIS et al. Title: Copper (II) complex of an estradiol derivative with potent antiinflammatory properties (Abstract only) Publ: Arch. Pharm. Vol/Iss: 324 (9) Pages: 533-536 Date: 1991			
	61	Author: WANG et al. Title: Photoaffinity labeling of human placental estradiol 17 β -dehydrogenase with 2- and 4-azidoestrone, 2- and 4-azidoestradiol (Abstract only) Publ: Shengwu Huaxue Zazhi Vol/Iss: 8 (6) Pages: 715-718 Date: 1992			
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	64	Author: WURTZ et al. Title: Three-Dimensional Models of Estrogen Receptor Ligand Binding Domain Complexes, Based on Related Crystal Structures and Mutational and Structure-Activity Relationship Data Publ: Journal of Medicinal Chemistry Vol/Iss: 41 Pages: 1803-1814 Date: 1998				

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